

Please add the following claims:

26. A method for identifying organic non-peptide compounds useful in the treatment of cancer comprising the step of contacting a mammalian protein of the p53 family, whether mutant or wild-type, with an organic non-peptide compound and determining whether said compound is capable of binding to one or more domains of said protein under physiological conditions and restoring or stabilizing a functional conformation therein.

27. The method of claim 26 wherein said protein is human.

28. The method of claim 27 wherein measurement of said conformation is performed by a method selected from the group consisting of chromatography, spectroscopy, absorption, ultracentrifugation, specific DNA binding assays, and protein binding of another gene product known to be inhibited or activated by p53.

29. The method of claim 27 wherein said protein is a full-length mutant p53 protein.

30. The method of claim 27 wherein the DNA binding domain of said p53 protein is destabilized compared to the wild-type.

31. The method of claim 27 wherein the DNA binding domain of said p53 protein has one or more mutations that render it susceptible to misfolding.

32. The method of claim 27 wherein the DNA binding domain of said p53 protein contains one or more mutations at one or more of residue positions 175, 245, 248, 249, 273, and 282.

33. The method of claim 27 wherein said protein is a p53 deletion derivative.

34. The method of claim 27 wherein said protein comprises the DNA binding domain of said p53 protein without the entire N and C terminal domains.

35. The method of claim 27 wherein the DNA binding domain of said p53 protein is wild-type.

36. The method of claim 27 wherein the DNA binding domain of said p53 protein contains a missense mutation.

37. The method of claim 27 wherein said protein of the p53 family is selected from the group consisting of p53, p63, and p73.

38. The method of claim 27 wherein the contacting and measuring steps are performed simultaneously by detecting a conformational change of said p53 protein in the presence of said compound.

39. The method of claim 27 wherein the compound is additionally screened *in vivo* for ability to halt or repress tumor growth.

40. The method of claim 27 further wherein the compound is additionally screened *in vitro* for ability to halt or repress tumor growth.

41. The method of claim 27 wherein said screening is performed using:
(a) tumor cells that express a mutant of p53 protein; or
(b) a cell line that expresses a mutant of p53 protein.
42. The method of claim 27 wherein the measurement of functional conformation is determined at a temperature of approximately 20°C to 50°C.
43. The method of claim 27 comprising anchoring the protein or the test compound onto a solid phase surface and detecting protein-compound complexes.
44. The method of claim 27 wherein the protein is anchored on a solid support and the compound is labeled.
45. The method of claim 44 wherein the label is a radioisotope or a fluorescent label.
46. The method of claim 27 wherein stabilization of functional p53 protein conformation is determined by anchoring said p53 protein, and a detectably-labeled conformationally-sensitive antibody whose binding to an epitope of p53 is dependent upon the presence of native p53 conformation, to a solid support in the presence, and also the absence, of said organic non-peptide compound, and measuring the amount of p53 and/or antibody that is bound to said solid support.
47. The method of claim 27 wherein a monoclonal antibody, specific for p53 DNA binding domain is used to anchor the protein to a solid phase surface.
48. The method of claim 27 wherein said step of determining binding capability and restoration of p53 functional conformation comprises the steps of: (1) contacting the p53 protein with an antibody that specifically recognizes a conformationally sensitive epitope of p53, and (2) determining whether said antibody binds to said protein in the presence of said organic non-peptide compound.
49. The method of claim 48 wherein the presence of epitope correlates with at least one wild-type physiological activity of p53.
50. The method of claim 48 wherein a defect in epitope correlates with at least one inactivated state of p53.
51. The method of claim 48 wherein a detectable label is additionally attached to said antibody by contacting said antibody with a further antibody that is detectably labeled.
52. The method of claim 48 wherein said antibody is mAb 1620 or mAb 240.
53. The method of claim 48 wherein the protein is a temperature sensitive mutant form of p53 possessing an epitope recognized by mAb 240.
54. The method of claim 48 wherein said compound interacts with a protein of the p53 family to restore or stabilize wild-type activity thereof, wherein said activity comprises tumor suppression activity.

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55. The method of claim 27 further comprising designing an additional compound that promote a wild-type activity of a protein of the p53 family wherein said compound is used to generate a hypothesis, identifying a candidate compound that fits the hypothesis, and determining if the candidate compound promotes a wild-type activity of the p53 family.

56. A method of evaluating whether an organic non-peptide compound can promote a wild-type activity in a mutant form of a mammalian protein of the p53 family, wherein one or more functional activities of said protein are at least partially impaired by the inability of said protein to maintain a functional conformation under physiological conditions, said method comprising the steps of:

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- (a) contacting said mutant protein with an organic non-peptide compound that is capable of binding to one or more domains in said mutant protein under physiological conditions and stabilizing a functional conformation therein; and,
 - (b₁) permitting said stabilized protein to interact with one or more macromolecules that participate in said wild-type activity with measurement of said activity; or
 - (b₂) confirming the presence of said functional conformation via a method selected from the group consisting of chromatography, spectroscopy, absorption, ultracentrifugation, specific DNA binding assays, and protein binding of another gene product known to be inhibited or activated by p53.
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